Reviewer Report

Title: **eModel-BDB: A database of comparative structure models of drug-target interactions from the Binding Database**

Version: **Original Submission**   **Date:** 11/22/2017

Reviewer name: **Janez Konc**

Reviewer Comments to Author:

The authors developed a database of drug-target models that cover the Binding Database that could be used in drug discovery - especially genome-wide virtual screening to support drug repurposing.SPECIFIC COMMENTS1. page 5, lines 1-22: It is not clear how BindingDB drugs are assigned to the predicted pockets with fingerprint-based virtual screening. How is the rank of the drug against pockets detect by eFindSite computed? This should be elaborated.2. page 5, lines 31-32: Why is global structure similarity measure (TM-score) used? To measure the quality of alignment of ligand-bound template binding sites onto the apo-binding site, using some local similarity measure would be better.3. page 7, lines 47-48: The median RMSD of 2.9 Å for the binding pocket (comparison between the generated model and experimental PDB structure) seems rather high. A comment should be added how this could affect drug discovery with docking approaches.4. page 8, lines 23-24: Several other pocket matching algorithms exist and have been used for drug discovery, but the authors provide only two of their own recent works (refs 24 and 25) currently at the submission stage. Consider discussing other successful recent examples as well. GENERAL COMMENTS1. Is the study accounting for biological assemblies, i.e., biologically relevant complexes of proteins? For example, many binding site pockets are between two proteins that form a protein-protein complex. Such pockets are only complete if both interacting protein structures are considered. If this is not the case, this may be a drawback. It should be discussed how biological assemblies were considered.

Level of Interest

Please indicate how interesting you found the manuscript: An article of importance in its field

Quality of Written English

Please indicate the quality of language in the manuscript: Acceptable

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